REMARKS

Applicants reply to the Final Office Action dated July 21, 2006, within two months. Thus, Applicants request an Advisory Action, if necessary. Claims 1-7, 9-12 and 14-16 were pending in the application and the Examiner rejects claims 1-7, 9-12 and 14-16. Support for the amendments may be found in the originally-filed specification, claims, and figures. No new matter has been introduced by these amendments. Applicants assert that the application is in condition for allowance and reconsideration of the pending claims is requested.

Rejection under 35 U.S.C. § 112

The Examiner rejects claims 1-7, 9-12 and 14-15 under 35 U.S.C. § 112, second paragraph, because the Examiner asserts that it is unclear what temperatures are considered a "non-denaturing temperature for cytokines." Applicants respectfully traverse this rejection.

Applicants assert that claim 1 as amended clarifies the range of temperatures that are encompassed by the term "non-denaturing temperature conditions". Support for 37°C is from, for example, page 63, line 7 of the English translation of the specification and the common general knowledge. One skilled in the art would know that any temperature below 37°C would not constitute heating (and would therefore be non-denaturing) for a biological sample. Support for the upper limit for a non-denaturing temperature range of 55°C can be found throughout the specification, such as, for example, page 63, lines 18-22 of the English translation of the specification.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejects claim 16 under 35 U.S.C. § 103(a) as being unpatentable over Yuan et al. or Matsumoto et al. in view of Pennanen et al. and further in view of Wagner et al. Applicants respectfully traverse this rejection.

The cited references have been summarized in previous instructions and hence will not be summarized herein. The Examiner asserts that Yuan et al. and Matsumoto et al. disclose a time resolved immunoassay method for detection of alpha-fetoprotein in a biological sample, and that the use of S-diketone ligand

improves detection sensitivity. The Examiner asserts that Pennanen et al. disclose detection of cytokines in a sample by time resolved fluoroimmunoassay, and Wagner et al. discloses packaging of immunoassay components in a kit format. As such, the Examiner asserts that claim 16 is obvious over the cited references.

Applicants also assert that the kit, as set forth in amended claim 16, is directed only to use with samples which have been heat treated. The incorporation of the step of heating the biological sample at a non-denaturing temperature is not taught or suggested by any of the cited references, and as such, *prima facie* obviousness clearly is not established. Applicants assert that where heat treatment of a sample to expose epitopes may be a routine modification, heat treatment under non-denaturing temperature conditions of about 37°C to about 55°C is not a routine modification. Specifically, such heat treatment would be assumed by one skilled in the art to be useless, as only by denaturation are additional epitopes exposed. As such, the Applicants' discovery that heating plasma samples under non-denaturing temperature conditions leads to increased sensitivity of detection (as evidenced in Figure 3b) is an unexpected advantage, and the obviousness rejection should thus be withdrawn.

Moreover, one skilled in the art would not think that the methods of the primary references would be applicable to low level analytes such as chemokines, as these methods are found to be highly sensitive for analytes already present at high levels.

Applicants reiterate that Yuan and Matsumoto, directed to the problem of detecting cytokines, disclose the use of a lanthanide chelating agent found to be sensitive when used in assays to *detect the tumor marker alpha-fetoprotein* (emphasis added). The skilled artisan would expect such a protein to be at a high concentration in the serum of the tumor-bearing patient, as the expression of tumor markers is up-regulated in such patients, and thus easy to detect. Therefore, any disclosure relating to the detection of such proteins would not lead one skilled in the art to assume that such could also be applied to chemokines, which have a low effective or free concentration in serum. As such, one skilled in the art would not be prompted to incorporate the solution to the problem of Yuan or Matsumoto, namely, the use of BHHCT, to the problem to be solved by the invention of the current

application. Applicants submit that the Examiner is using impermissible hindsight to assert that the cited prior art references would be obvious to one skilled in the art to combine to practice the present invention.

Based on the Examiner's previous remarks, one skilled in the art would assume that a method of detection even more highly sensitive than those disclosed in the primary references would be required to detect a chemokine. As such, the success of the claimed invention for detecting chemokines must be considered an unexpected achievement thereby, obviating the Examiner's obviousness assertion.

Wagner *et al.* discloses a method and materials for immunoassay which does not require separation of bound and free fractions; it is directed towards homogeneous fluorescence immunoassay. As such, Wagner is non-analogous art as it merely discloses an immunoassay in kit format for detection of chemokines in biological samples. As there would be no reason to apply the methods of the primary references to detection of a chemokine, as discussed above, the invention of a kit for detecting chemokines using such methods must be likewise non-obvious.

Clarification in the Specification

The Examiner asserts that page 63, lines 12-16 of the specification are contrary to our arguments and requests clarification. Applicants assert that the statement on page 63, lines 12-16 of the English translation which recites "heating at 37°C or 55°C for 30 minutes yielded... of SDF-1", is in reference to analysis of SDF-1 reference solutions, not plasma samples. Furthermore, as heating reference samples at 37°C or 100°C actually decreased the amount detected, this recitation is not contrary to our arguments.

CONCLUSION

Applicants respectfully submit that the pending claims are in condition for allowance. The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account No. **19-2814**. Applicants invite the Examiner to telephone the undersigned if the Examiner has any questions regarding this Reply or the present application in general.

Respectfully submitted,

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By: _____
Howard I. Sobelman
Reg. No. 39,038

SNELL & WILMER L.L.P.
One Arizona Center
400 East Van Buren
Phoenix, Arizona 85004-2202
Phone: (602) 382-6228
Fax: (602) 382-6070
Email: hsobelman@swlaw.com